

What is claimed is

1. A compound for inhibiting expression of angiogenin comprising an oligonucleotide or analog thereof having a base sequence complementary to a target portion of a nucleic acid encoding angiogenin.

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2. The compound of claim 1 wherein the base sequence is configured to bind to the target portion of the nucleic acid in a manner to inhibit the expression of angiogenin.

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3. The compound of claim 2 wherein the oligonucleotide analog comprises a modified internucleotide linkage, a modified purine or pyrimidine moiety, a modified sugar moiety, a modified 5' hydroxyl moiety, a modified 3' hydroxyl moiety or a modified 2' hydroxyl moiety.

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4. The compound of claim 3 wherein the modified internucleotide linkage comprises a substituent having an improved aqueous or lipid solubility or improved resistance to nuclease digestion.

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5. The compound of claim 4 wherein the modified internucleotide linkage is selected from the group consisting of phosphorothioate, alkyl or cycloalkyl phosphorothioate, N-alkyl or cycloalkyl phosphoramidates, phosphorodithioates, alkyl or cycloalkyl phosphonates, phosphodiester, phosphotriester, C<sub>1</sub> - C<sub>4</sub> alkyl,



CF<sub>3</sub>, OCF<sub>3</sub>, O, S, or N-alkyl; O, S, or N-alkenyl; SOCH<sub>3</sub>; SO<sub>2</sub>CH<sub>3</sub>; ONO<sub>2</sub>; NO<sub>2</sub>; N<sub>3</sub>; NH<sub>2</sub>; heterocycloalkyl or alkaryl; aminoalkylamino; polyalkylamino; substituted silyl; an RNA cleaving group; a cholesteryl group; a conjugate; a reporter group; an intercalator; a group for improving the pharmacokinetic properties of an oligonucleotide; and a group for improving the pharmacodynamic properties of an oligonucleotide.

10. The compound of claim 1 wherein the base sequence of the oligonucleotide or analog thereof is selected from the group consisting of

5'-GCCCCATCACCATCTCTTC-3',

5'-ACACGGCATCATGAATCA-3',

5'-CCAGGGGGCCCGCTGGTTA-3',

5'-ACCAAATTTTATATTCTA-3',

5'-CAGGCCCATCACCATCAC-3',

5'-GCCCAGGCCCATCACCAT-3', and

5'-TCTCTGACACGGCATCAT-3'.

11. A composition for inhibiting expression of angiogenin comprising an effective amount of an oligonucleotide or analog thereof having a base sequence complementary to a target portion of a nucleic acid encoding angiogenin in a pharmaceutically acceptable carrier.

12. The composition of claim 11 wherein the base sequence of the oligonucleotide or analog thereof is selected from the group consisting of

5'- GCCCATCACCATCTCTTC - 3',

5'- ACACGGCATCATGAATCA - 3',

5'-CCAGGGGCCCCGCTGGTTA-3',

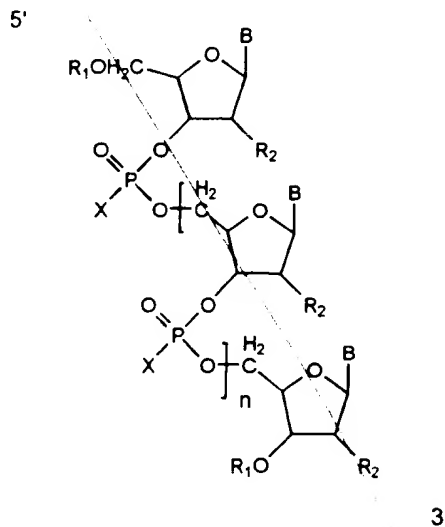
5'-ACCAAATTTTATATTCTA-3',

5'-CAGGCCCATCACCATCAC-3',

5'-GCCCAGGCCCATCACCAT-3', and

5'-TCTCTGACACGGCATCAT-3'.

13. A compound for inhibiting expression of angiogenin having the formula:



wherein

X is O, S, or C<sub>1-4</sub> alkyl;

B is adenine, guanine, cytosine, or thymine selected such that the oligonucleotide has a complementary base sequence with a portion of a target nucleic acid strand coding for angiogenin thereby inhibiting expression thereof;

5  $R_1$  is H,  $C_{1-4}$  alkyl, intercalating agent, peptide, enzyme, ribozyme, substituted acridine, 2-methoxy-6-chloro-9-pentylaminoacridine, N-(6-chloro-2-methoxyacridinyl)-O-methoxydisopropylaminophosphinyl-3-aminopropanol and N-(6-chloro-2-methoxyacridinyl)-O-methoxydisopropylaminophosphinyl-5-aminopentanol or substituted acridine;

10  $R_2$  is H, OH, SH,  $SCH_2$ ,  $OCH_3$ , F, OCN,  $OCH_2CH_3$ ,  $OCH_2OCH_3$ ,  $OCH_2O(CH_2)_nCH_3$ ,  $O(CH_2)_nNH_2$  or  $O(CH_2)_nCH_3$  where n is from 1 to about 10;  $C_1$  to  $C_{10}$  lower alkyl, substituted lower alkyl, alkaryl or aralkyl; Cl; Br; CN;  $CF_3$ ;  $OCF_3$ ; O, S, or N-alkyl; O, S, or N-alkenyl;  $SOCH_3$ ;  $SO_2CH_3$ ;  $ONO_2$ ;  $NO_2$ ;  $N_3$ ;  $NH_2$ ; heterocycloalkyl or alkaryl; aminoalkylamino; polyalkylamino; substituted silyl; an RNA cleaving group; a cholesteryl group; a conjugate; a reporter group; an intercalator; a group for improving the pharmacokinetic properties of an oligonucleotide; or a group for improving the pharmacodynamic properties of an oligonucleotide; and

n is 5 to 100.

20 14. The compound of claim 13 wherein the base sequence is selected from the group consisting of  
5'-GCCCATCACCATCTCTTC-3',

5'-ACACGGCATCATGAATCA-3',

5'-CCAGGGGCCCCGCTGGTTA-3',

5'-ACCAAATTTTATATTCTA-3',

5'-CAGGCCCATCACCATCAC-3',

5'-GCCCAGGCCCATCACCAT-3', and

5'-TCTCTGACACGGCATCAT-3'.

15. A method for inhibiting expression of angiogenin in a mammal comprising administering to the mammal an effective amount of an oligonucleotide or analog thereof having a base sequence complementary to a target portion of a nucleic acid encoding angiogenin so as to inhibit the expression of angiogenin.

16. A method for reducing size of tumors associated with angiogenesis in a mammal comprising administering to the mammal an effective amount of an oligonucleotide or analog thereof having a base sequence complementary to a target portion of a nucleic acid encoding angiogenin so as to reduce tumor size.

17. A method for decreasing production of angiogenin in a mammal comprising administering to the mammal an effective amount of an oligonucleotide or analog thereof having a base sequence complementary to a target portion of a nucleic acid encoding angiogenin so as to decrease production of angiogenin.

18. A method for inhibiting metastasis of tumor cells in a mammal comprising administering to the mammal an effective amount of an oligonucleotide or analog thereof having a base sequence complementary to a target portion of a nucleic acid encoding angiogenin so as to inhibit metastasis of tumor cells.

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19. A method for inhibiting the establishment of tumor cells in a mammal comprising administering to the mammal an effective amount of an oligonucleotide or analog thereof having a base sequence complementary to a target portion of a nucleic acid encoding angiogenin so as to inhibit establishment of tumor cells.

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20. A method for inhibiting growth of tumors associated with angiogenesis in a mammal comprising administering to the mammal an effective amount of an oligonucleotide or analog thereof having a base sequence complementary to a target portion of a nucleic acid encoding angiogenin so as to inhibit tumor growth.

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21. A method for detecting the presence of angiogenin in a sample comprising contacting the sample with a labeled oligonucleotide or analog thereof having a base sequence complementary to a target portion of a nucleic acid encoding angiogenin;

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allowing the labeled oligonucleotide or analog thereof to bind to the target portion of the nucleic acid encoding angiogenin; and

detecting the labeled oligonucleotide or analog thereof.

22. A method for detecting the presence of angiogenin in a mammal comprising administering to the mammal a labeled oligonucleotide or analog thereof having a base sequence complementary to a target portion of a nucleic acid encoding angiogenin;

5                   allowing the labeled oligonucleotide or analog thereof to bind to the target portion of the nucleic acid encoding angiogenin; and  
                  detecting the labeled oligonucleotide or analog thereof.

23. A method for diagnosing conditions associated with abnormal angiogenesis in a mammal comprising administering to the mammal a labeled oligonucleotide or analog thereof having a base sequence complementary to a target portion of a nucleic acid encoding angiogenin;

10                   allowing the labeled oligonucleotide or analog thereof to bind to the target portion of the nucleic acid encoding angiogenin;

15                   detecting the labeled oligonucleotide or analog thereof;

                  measuring the labeled oligonucleotide or analog thereof; and

                  determining the abnormal condition based on the detecting and measuring of the labeled oligonucleotide or analog thereof.

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